REMARKS

The Office action dated September 30, 2009 is acknowledged. The Applicants thank the Examiner for the entry of the previously filed Request for Continued Examination (RCE). Claims 1 and 3-6 and 8-36 are pending in the instant application. Claims 1, 3-6, 8-14, 20-29 and 33-35 have been rejected and claims 15-19, 30-32 and 36 have been withdrawn. By the present Office Action response, claims 1, 8, 9 and 24 have been amended and claims 3, 12 and 20 have been cancelled. Claim 1 has been amended to incorporate most of the limitations of canceled claim 3 and to recite that the administration form is multilayered (support for which may be found throughout the specification, such as at paragraph [00024]). Claims 8, 9 and 24 have been amended for clarification purposes. Reconsideration is respectfully requested in light of the amendments and arguments made herein. No new matter has been added.

Rejection of claim 3 under 35 U.S.C. 112, first paragraph

The Examiner has rejected claim 3 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement in that the claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. In particular, the Examiner states that none of the cellulose derivatives, other than those listed in claim 20, and none of the starch derivatives meet the written description requirement due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The Applicants submit that claim 3 has been canceled and the relevant limitations thereof have been incorporated into claim 1.

Therefore, withdrawal of this rejection is requested.

Rejection of claims 1, 3-6, 8-14, 20-29 and 33-35 under 35 U.S.C. 112, second paragraph

The Examiner has rejected claims 1, 3-6, 8-14, 20-29 and 33-35 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. In particular, the Examiner states that line 11 of claim 1 recites "said pH being," but it is unclear whether "said pH" refers to the pH value of the base mass (claim 9) or the physiological pH of the mucosa to which the administration form is to be applied (lines 10-11). Claims 24 and 25 are also rejected as being dependent from canceled claim 7.

Claim 1 has been amended to clarify that the pH refers to the pH value of the mucosa to which the administration form is to be applied and to which the pH value of the base mass for producing said administration form is approximated or adapted. Support may be found throughout the specification, such as at paragraphs [000019] and [000020].

Claim 24 has been amended accordingly and claim 25 depends from claim 24.

Withdrawal of this rejection is requested.

Rejection of claims 1, 3-5, 8-11, 13, 14, 20-22, 24-29, 33 and 34 under 35 U.S.C. 102(b)

Claims 1, 3-5, 8-11, 13, 21, 22, 24-26 and 29 have been rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 4,572,832 (Kigasawa, et al.). The Examiner maintains the rejection as set forth in the previous Office action. In particular, the Examiner states that Kigasawa, et al. disclose every limitation recited in the

aforementioned claims, namely, soft buccal compositions which comprise a medicament to be absorbed through the oral cavity, a water-soluble protein, a polyhydric alcohol and a fatty acid ester and/or a carboxyvinyl polymer. The Examiner also believes that the reference discloses a soft buccal comprising the active ingredient pindolol which is prepared using the film forming polymer gelatin (gelatine), pH 6.5 phosphate buffer and the excipients propylene glycol, medium-chain fatty acid triglycerides, sucrose fatty acid ester, glycerin, mannitol and corn starch (col. 12, lines 43-60; Example 8). The Examiner further states that the total weight of the excipients is about 70% of the total weight of the product and that after sonication to create a dispersion, the gelatin was added and the resulting mixture kneaded and cut into plate-shaped (i.e., a film-shaped) dosage form, which took between 16 minutes and 17 minutes - 15 seconds to disintegrate. The Examiner thus concludes that Kigasawa, et al. teach a film-shaped, dried dosage form comprising an active ingredient and at least one matrix-forming polymer whose pH value is adapted to the physiological pH value of the mucosa to which the administration form is to be applied.

The Applicants respectfully disagree with the Examiner's conclusion and submit that the present invention as defined in the present claims is patentably distinct from the invention disclosed in the prior art Kigasawa, et al. reference. Present claim 1, as amended herewith, recites a multi-layered, film-shaped administration form for transmucosal administration of an active substance contained in said administration form wherein said administration form comprises a base mass for producing said administration form, said base mass comprising at least one matrix-forming polymer selected from the group consisting of pullulan, polyacrylamides, alginates, chitosan,

alginic acid, arabinogalactan, galactomannan, agar-agar, agarose and carrageenan. The base mass further comprises at least one active substance. The base mass has a pH value in the presence of water or of a water-containing solvent mixture, wherein during the production of the administration form, the pH value of the base mass for producing the administration form is approximated or adapted to the physiological pH value of the mucosa to which the administration form is to be applied, the pH being at 8-9 when the mucosa is a herbivoral mucosa, between 5.5-6.5 when the mucosa is a human oral mucosa, at about 6 when the mucosa is a human nasal mucosa or at about 4 when the mucosa is a human vaginal mucosa. The at least one active substance is selected from the group consisting of pharmaceutically active substances and aroma substances.

It is submitted that Kigasawa, et al. teach a soft buccal containing (1) a medicament to be absorbed through the oral mucosa, (2) a water-soluble protein, for example, gelatine, casein, solubilized collagen and glue, (3) a polyhydric alcohol, for example, propylene glycol, butylenes glycol, polyethylene glycol, glycerol, trimetylolpropane, polyvinyl alcohol, cellulose derivatives, sugars, and (4) a fatty acid ester and/or a carboxyvinyl polymer. The Applicants respectfully submit that Kigasawa, et al. fail to teach that the soft buccal administration form may contain a matrix-forming polymer selected from the group consisting of pullulan, polyacrylamides, alginates, chitosan, alginic acid, arabinogalactan, galactomannan, agar-agar, agarose and carrageenan. Moreover, the reference fails to teach that the soft buccal may be multilayered. Therefore, Kigasawa, et al. fail to teach each and every limitation of present claim 1 as amended herewith.

Claims 1, 3-5, 9-11, 13, 14, 20, 22, 24, 25, 27-29, 33 and 34 have been rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 4,764,378 (Keith, et al.). The Examiner argues that Keith, et al. disclose buccals dosage forms for transmucosal administration of drugs and thus the pH of the base mass of these dosage forms is approximated or adapted to the physiological values of the mucosa to which the administration form is to be applied and that the base bass PEG (polyethylene oxide) of varying molecular weights (100, 1450, 3350 and 8000), propylene glycol (a plasticizer) and polyvinylpyrrolidone that when cut in a film dissolves in less than 60 seconds when placed in the buccal pouch or sublingually. The Examiner also states that the reference teaches that the base mass contains 5% of the plasticizer propylene glycol and that a variety of pharmaceutical active ingredients can be incorporated in the base material, including 5% verapamil hydrochloride, a hydrochloride salt form of the active ingredient, resulting in a final formulation in which the polymer portion would be less than 95% (5% active ingredient, 3% propylene glycol).

The Applicants respectfully disagree with the Examiner's conclusion regarding Keith, et al. as well and submit that the present invention as defined in the present claims is patentably distinct from the invention disclosed in the prior art Keith, et al. reference. It is submitted that Keith, et al. teach buccal dosage forms for transmucosal administration of drugs, wherein a pharmaceutical compound is dispersed in an erodible matrix comprising about 20 to 75%-wt. of a low molecular weight polyethylene component, about 2 to 65%-wt. of a medium or high molecular weight polyethylene glycol and from about 1 to about 40%-wt. of an auxiliary high molecular weight polymer, preferably selected from the group consisting of polyethylene oxide and polyvinyl

pyrrolidone.

The Applicants respectfully submit that Keith, et al. fail to teach that the buccal dosage form may comprise a polymer selected from the group consisting of pullulan, polyacrylamides, alginates, chitosan, alginic acid, arabinogalactan, galactomannan, agar-agar, agarose and carrageenan. Moreover, the reference fails to teach that the buccal dosage form may be multilayered. Therefore, Keith, et al. fail to teach each and every limitation of present claim 1 as amended herewith.

In view of the above, it is submitted that neither Kisagawa, et al. nor Keith, et al. teach every limitation of present claim 1. Therefore, neither reference anticipates the presently claimed invention as recited in claim 1. Withdrawal of these rejections is requested.

Rejection of claims 1, 3-6, 8-14, 20-29 and 33-35 under 35 U.S.C. 103(a)

Claims 1, 3-6, 8-11, 13, 14, 20-29 and 33-35 have been rejected as being unpatentable over Kigasawa, et al. for the reasons set forth in the previous Office action. In particular, the Examiner states that Kigasawa, et al. disclose soft buccal compositions which comprise a medicament to be absorbed through the oral cavity, a water-soluble protein, a polyhydric alcohol and a fatty acid ester and/or a carboxyvinyl polymer. The Examiner also states that forms include sheets, bands and disks. The Examiner further states that the reference discloses a soft buccal comprising the active ingredient pindolol which is prepared using the film forming polymer gelatin (gelatine), pH 6.5 phosphate buffer and the excipients propylene glycol, medium-chain fatty acid triglycerides, sucrose fatty acid ester, glycerin, mannitol and corn starch. The Examiner still further states that the total weight of the excipients is about 70% of the total weight of the product and that

after sonication to create a dispersion, the gelatin was added and the resulting mixture kneaded and cut into plate-shaped (i.e., a film-shaped) dosage form, which took between 16 minutes and 17 minutes, 15 seconds to disintegrate. The Examiner thus concludes that Kigasawa, et al. teach a film-shaped, dried dosage form comprising an active ingredient and at least one matrix-forming polymer whose pH value is adapted to the physiological pH value of the mucosa to which the administration form is to be applied.

The Examiner states that Kigasawa, et al. fail to explicitly prepare administration forms which contain aroma substances or cellulose derivatives or an administration form which disintegrates in less than 10 minutes. However, the Examiner argues that Kigasawa, et al. does disclose that additives can be added in addition to the required ingredients, including flavorings (i.e., aroma substances), such as menthol, lemon oil and citrus flavors, as well as other excipients, disintegrating adjusting agents, emulsifiers, dispersants, binders and thickeners. Additionally, the Examiner states that the reference discloses that for the required polyhydric alcohol component, ingredients can be ethylene glycol, propylene glycol or polyethylene glycol, and that included in the category of polyhydric alcohols are cellulose and cellulose derivatives such as methyl cellulose, ethyl cellulose, hydroxymethyl cellulose, hydroxyethyl cellulose and carboxymethyl cellulose.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a dosage form with an aroma ingredient, taught by Kigasawa, et al., as an ingredient to impart a flavor/aroma to the medicament and to use a cellulose derivative such as ethyl cellulose for the required polyhydric alcohol component of the film administration. The Examiner also states that the amount of an aroma ingredient in a composition is clearly a result effective parameter that one

skilled in the art would routinely optimize, and the aroma/flavor chosen and the strength of the aroma/flavor desired or required in the composition, such as to mask the taste of a bitter active ingredient, would determine the amount of the ingredient present in the composition. The Examiner further states that one skilled in the art would adjust the composition of the tablet in order to provide a fast disintegration of the dosage form to minimize the possibility for swallowing the dosage form and losing the benefits of the buccal administration form.

Regarding claims 33 and 34, the Examiner states that Kigasawa, et al. teach that pharmaceutically active ingredients in the salt form are suitable for incorporation into the soft buccal form and that the salts triperizone hydrochloride, dantrolene sodium, cyclobenzaprine hydrochloride and ipratroprium bromide are exemplified. The Examiner further states that menthol (which reads on aroma substance) can be included in the soft buccal dosage form. Therefore, the Examiner concludes that a dosage with only menthol in the base mass will meet the limitation of claim 35 in which the active substance present in the film-shaped administration form is an aroma substance.

Claims 1, 3-6, 8-11, 13, 14, 20-29 and 33-35 have been rejected as being unpatentable over Kigasawa, et al., as applied to claims 1, 3-6, 8-11, 13, 14, 20-29 and 33-35 above, and further in view of U.S. Publication No. 2003/0099691 (Lydzinski, et al.). In particular, the Examiner states that Kigasawa, et al. disclose soft buccal compositions which comprise a medicament to be absorbed through the oral cavity, a water-soluble protein, a polyhydric alcohol and a fatty acid ester and/or a carboxyvinyl polymer, as well as that additives can be added in addition to the require ingredients, including flavorings, such as menthol, lemon oil and citrus flavor, as well as other

excipients, disintegrating adjusting agents, emulsifiers, dispersants, binders and thickeners. However, the Examiner states that Kigasawa, et al. fail to disclose a formulation wherein the substance is one or more aroma substances without a pharmaceutical active substance being included in the administration form.

The Examiner refers to Lydzinski, et al. and states that the reference discloses an oral film that is useful for delivering an agent to an animal or human to produce either a therapeutic or cosmetic effect, such as breath fresheners or fragrances and that the active agent can be used in any amount desired, the only limitation being the potential load of the film, but generally that the amounts used will range from about 0.5% to about 15%, with substantially higher amounts for breath fresheners than for pharmaceutical agents.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate an aroma substance in place of the pharmaceutically active ingredient in the compositions of Kigasawa, et al. with the motivation that it would have been reasonable to have expected success since the inclusion of an aroma substance results in an oral film that quickly disintegrates in the mouth, leaving the user with fresh or scented breath. Moreover, the Examiner states that as Lydzinski, et al. teach, almost any amount of active substance can be present in the film and the type of active ingredient will determine how much is added, with pharmaceutically active substances generally present in lower amounts than breath freshener ingredients.

Claims 1, 3-6, 8-14, 20-29, 33 and 34 have been rejected as being unpatentable over Kigasawa, et al., and further in view of U.S. Patent No. 5,900,247 (Rault, et al.) for the reasons set forth in the previous Office action. In particular, the Examiner states that

Kigasawa, et al. disclose soft buccal administration forms of active ingredients that can be formulated as disks or wafers, as discussed above. However, the Examiner states that Kigasawa, et al. fail to disclose a multilayer dosage form.

The Examiner refers to Rault, et al. and states that the reference discloses a bioadhesive pharmaceutical composition to locally release active ingredients through various mucosal membranes, and that the bioadhesive composition comprises a vinyl acetate/polyvinylpyrrolidinone copolymer, at least one active ingredient, optionally a cellulose or cellulose derivative such as ethyl cellulose or hydroxypropylmethyl cellulose and excipients such as plasticizers, flavoring agents or sweeteners. The Examiner further states that after spreading of the bioadhesive mixture onto a biodegradable or non-biodegradable protective film or substrate, the assembly is dried and the protective film is chosen for its adhesive or bioadhesive properties and is peelable. According to the Examiner, this process results in the production of a multilayered administration form and that in Example 4 of the reference, a composition is prepared which contains approximately 3% by dry weight of flavoring agents.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a buccal administration form as taught by Kigasawa, et al. and to place this material on a protective film as taught by Rault, et al., resulting in a multilayered administration form. The Examiner also concludes that Rault, et al. provide additional guidance to one skilled in the art as to the amount of flavoring ingredients, which can include aroma substances, that can be added to such compositions.

Claims 1, 3-5, 9-11, 13, 14, 20-22, 24, 25, 27-29, 33 and 34 have been rejected as being unpatentable over U.S. Patent No. 4,764,378 (Keith, et al.). In particular, the

Examiner states that Keith, et al. disclose buccals dosage forms for transmucosal administration of drugs, and thus the pH of the base mass of these dosage forms is approximated or adapted to the physiological values of the mucosa to which the administration form is to be applied and in the amounts listed on page 12 of the Office action. The Examiner states that Keith, et al. fail to disclose an administration form wherein the polymer portion ranges between 15% and 75%, but concludes that it would have been obvious to one skilled in the art to vary the amounts of polymer matrix, active ingredients and additional ingredients in the buccals dosage form. The Examiner further states that optimization of parameters is a routine practice that would be obvious to one skilled in the art to employ and reasonably would expect success. Thus, the Examiner states that the amount of plasticizer or various polymer ingredients will alter the physical properties of the produced mass, such as the melting point, crystalline character and disintegration time.

Claims 1, 3-5, 9-14, 20-22, 24, 25, 27-29, 33 and 34 have been rejected as being unpatentable over Keith, et al. as applied to claims 1, 3-5, 9-11, 13, 14, 20-22, 24, 25, 27-29, 33 and 34 above, and further in view of Rault, et al. In particular, the Examiner states that Keith, et al. disclose buccals dosage forms containing up to 10% by weight active ingredient, in a matrix-forming polymer mass but fail to disclose a multi-layer dosage form.

The Examiner refers to Rault, et al. for disclosing a bioadhesive pharmaceutical composition to locally release active ingredients through various mucosal membranes, and that the bioadhesive composition comprises a vinyl acetate/polyvinylpyrrolidinone copolymer, at least one active ingredient, optionally a cellulose or cellulose derivative

such as ethyl cellulose or hydroxypropylmethyl cellulose and excipients such as plasticizers, flavoring agents or sweeteners. The Examiner further states that after spreading of the bioadhesive mixture onto a biodegradable or non-biodegradable protective film or substrate, the assembly is dried and the protective film is chosen for its adhesive or bioadhesive properties and is peelable. According to the Examiner, this process results in the production of a multilayered administration form.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a buccal administration form as taught by Keith, et al. and to place this material on a protective film as taught by Rault, et al., resulting in a multilayered administration form.

Claims 1, 3-5, 8-11,13, 14, 20-22, 24, 25, 27-29, 33 and 34 have been rejected as being unpatentable over Keith, et al. as applied to claims 1, 3-5, 9-11, 13, 14, 20-22, 24, 25, 27-29, 33 and 34 above, and further in view of WO 99/53897 (Bergeron, et al.) and EP 0386960 (Gibson, et al.). In particular, the Examiner states that Keith, et al. disclose buccals dosage forms containing up to 10% by weight active ingredient, in a matrix-forming polymer mass but fail to disclose the presence of an agent that alters the pH from the Markush group of claim 8.

The Examiner refers to Bergeron, et al. for disclosing a formulation of film-forming ingredient and an active agent for topical formulations and that the pH of the formulation can be adjusted to meet the requirements of the target tissue. For example, formulations applied to the vaginal mucosa a pH of about 4.0-4.5 should be used. The Examiner points out that Bergeron, et al. fail to disclose any agents that would adjust the pH depending on the target tissue.

The Examiner refers to Gibson, et al. for disclosing that the pH of the compositions can be adjusted through the use of pharmaceutically acceptable acids or bases such as sodium or hydrochloric acid and that pH can be maintained by the use of buffering agents.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a pH adjusting agent in the compositions of Keith, et al. in view of the teachings of Bergeron, et al. and Gibson, et al.

Claims 1, 3-5, 9-11,13, 14, 20-22, 24, 25, 27-29, 33 and 34 have been rejected as being unpatentable over Keith, et al. as applied to claims 1, 3-5, 9-11, 13, 14, 20-22, 24, 25, 27-29, 33 and 34 above, and further in view of Lydzinski, et al. In particular, the Examiner states that Keith, et al. disclose buccals dosage forms containing up to 10% by weight active ingredient, in a matrix-forming polymer mass and that the active ingredients are pharmaceutically active compounds like scopolamine or verapamil hydrochloride. The Examiner states that the reference fails to disclose a formulation wherein the active substance is one or more aroma substances without a pharmaceutical active substance being included in the administration form.

The Examiner refers to Lydzinski, et al. for disclosing an oral film that is useful for delivering an agent to an animal or human to produce either a therapeutic or cosmetic effect, such as breath fresheners or fragrances, both of which allegedly read on the aroma substance of the instant claims.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate an aroma substance in place of the pharmaceutically active ingredient in the compositions of Keith, et al. in view of the

teachings of Lydzinski, et al.

It is respectfully submitted that to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The Applicants respectfully submit that one skilled in the art would have no suggestion or motivation to combine the aforementioned references in order to arrive at the present invention. Additionally, even if one skilled in the art were to consider the teachings of the cited prior art alone or in combination, each and every limitation of the present invention would not be disclosed, nor would there be a reasonable expectation of success if the aforementioned references were to be considered.

The Applicants respectfully disagree with the Examiner's position for at least the numerous deficiencies of Kigasawa, et al. and Keith, et al. discussed above. Moreover, none of the cited secondary references make up for any of the numerous deficiencies of Kigasawa, et al. and Keith, et al. Therefore, the combination of teachings of the references fails to teach every limitation of the present claims, and thus fail to render the presently claimed invention obvious. In particular, no combination of teachings of the references would render obvious to one skilled in the art a multi-layered, film-shaped administration form for transmucosal administration of at least one active substance, said administration form being applied to the oral mucosa of a herbivore, to the human oral mucosa, to the human nasal mucosa or to the human vaginal mucosa and wherein said administration form comprises a base mass for producing said administration form, said

base mass comprising at least one matrix-forming polymer selected from the group consisting of pullulan, polyacrylamides, alginates, chitosan, alginic acid, arabinogalactan, galactomannan, agar-agar, agarose and carrageenan, wherein the base mass has a pH value in the presence of water or of a water-containing solvent mixture, wherein during the production of the administration form, the pH value of the base mass for producing the administration form is approximated or adapted to the physiological pH value of the mucosa to which the administration form is to be applied, the pH being at 8-9 when the mucosa is a herbivoral mucosa, between 5.5-6.5 when the mucosa is a human oral mucosa, at about 6 when the mucosa is a human nasal mucosa or at about 4 when the mucosa is a human vaginal mucosa, and where the at least one active substance is selected from the group consisting of pharmaceutically active substances and aroma substances.

In view of the above, the Applicants respectfully request that the obviousness rejections be withdrawn.

Conclusion

For the foregoing reasons, it is believed that the present application, as amended, is in condition for allowance, and such action is earnestly solicited. Based on the foregoing arguments, amendments to the claims and deficiencies of the prior art references, the Applicants strongly urge that the obviousness-type rejection and anticipation rejections be withdrawn. The Examiner is invited to call the undersigned if

there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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By: _____
D. Peter Hochberg
Reg. No. 24,603

D. Peter Hochberg Co., L.P.A.
1940 East 6th Street, 6th Floor
Cleveland, OH 44114
(216) 771-3800